REMARKS

Reconsideration of the Examiner's rejections is respectfully requested. Claims 22, 30, 32, 41, 42, 45, 48, 49, and 58-66 are pending. Claims 1-21, 23-29, 31, 33-40, 43-44, 46-47, 50-57 have been cancelled. Inventorship has not been affected by the cancelled claims. Claim 30 is amended to correct a typographical error. Claim 63 is amended for technical clarity. No new matter has been added as a result of these amendments.

Applicants have not dedicated or abandoned any unclaimed subject matter and have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Claim Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 22, 30, 32, 41, 42, 45, 48, 49, and 58-66 are rejected as failing to comply with the written description requirement. Applicants respectfully disagree.

1. Patentability of a product may be based on a novel function.

In the August 9, 2006 Office Action, the Examiner states that for product claims, patentability is dependent solely upon the components present in the product, regardless of whether the product has a novel function. However, Applicants respectfully submit that functional language is not only permissible, but suggested in the instant application to accurately describe the novelty of the invention.

It is settled law that patentability of a product is not limited to the identity of its components. Rather, patentability may also turn on a unique function of the product's components. In *In Re Schreiber*, the Federal Circuit stated that "a patent applicant is free to recite features of an apparatus either structurally or functionally." 128 F.3d 1473, 1478 (Fed. Cir. 1997). In addition, the court in *In Re Swinehart* found that "there is nothing intrinsically wrong with [defining something by what it does rather than what it is] in drafting patent claims." 169 U.S.P.Q. 226, 228 (CCPA 1971).

In fact, the court encourages the use of functional language to determine patentability where it is impractical to define the product's feature based on structure. In *Rohm & Haas Co. v. Crystal Chem. Co.*, the court held that "[t]he use of functional language to claim an invention is specifically approved by statute, the patent office, and the courts, particularly where, as here, it is obviously impossible to

enumerate all possible combinations of weeds, crops, and application rates of propanil which will produce the recited useful selective post-emergence activity." 722 F.2d 1556 (Fed. Cir. 1983).

In the instant application, the Applicants define the novelty of the claimed invention by the fact that T1 changes as a result of cleavage of the claimed peptide with caspase. Under *Schreiber* and *Swinehart*, this functional definition is proper. Moreover, definition by function is necessary here, as it was in *Rohm & Haas*, because it would be overly cumbersome to enumerate all possible MRI agent combinations comprising peptides that contain the caspase cleavage sequence needed to produce the recited useful change in T1. Consequently, Applicants respectfully request the withdrawal of rejection on these grounds.

2. The Characteristics of Caspase-Cleavable Peptides that Render them Compatible with the Instant Invention are Known in the Art.

The Examiner also made a section 112 First Paragraph rejection based on the contention that the Applicant cannot randomly select peptides of the prior art and insert them into the instant invention without disclosing what makes them compatible with the instant invention. The Examiner reasoned that the reader cannot be assured based on the written description that the Inventor actually had possession and knowledge of the unique composition and/or method for which patent protection is sought. The Applicants respectfully submit, however, that the Applicants are not required to specify what makes the caspase-cleavable peptides compatible with the present invention because such knowledge was readily available to persons of ordinary skill in the art at the time the application was filed.

M.P.E.P. § 2163.02 states that:

> the objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.' In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed."

Where an application claims a specific functional product, the Federal Circuit holds that persons skilled in the art would recognize that the inventor had possession of the claimed invention, even where the inventor does not list in the specification any particular coding sequences or structures that give rise to the functional product, if such sequences or structures were known in the field at the time of

application. In *Capon v. Eshha*, 76 USPQ2d 1078, 1087 (Fed. Cir. 2005), the court held that the inventors could properly "claim novel genetic material described in terms of the functional characteristics of the protein it encodes," without including any complete sequences in the specification, because such sequences were "already known in the field." *Capon*, 76 U.S.P.Q.2d at 1083, 1087. Similarly, in *In Re Barr* the court held that "since the claimed compounds are composed of known classes of radicals, these radicals can be specified in terms of their function without recitation of structure." 444 F.2d 588, 593 (CCPA 1971).

Like the genetic sequences in *Capon* and the classes of radicals in *Barr*, the instant application claims peptide sequences in terms of their functional characteristics, in particular, their ability to be cleaved by the target protease caspase. This method of claiming is proper because, as presented in detail below, sequences that possess the claimed functional characteristics were "already known in the field" at the time of application. *See Capon*, 76 U.S. P.Q.2d at 1087.

A large body of scientific journal articles demonstrate that the requirements for caspase cleavage were known in the art at the time of application. Two are attached as exhibits A and B. In Sleath et al., *Substrate Specificity of the Protease That Processes Human Interleukin-1β*, 265 J. Biol. Chem. 14526, 14527 (1990) (Exhibit A), the authors reported that caspase has a "highly restricted substrate specificity," and presented data that detail the characteristics of peptides that are required for cleavage by caspase, including amino acid sequence, tertiary structure, and peptide length. In Howard et al., *IL-1-Converting Enzyme Requires Aspartic Acid Residues For Processing of the IL-1β Precursor At Two Distinct Sites and Does Not Cleave 31-kDa IL-1α*, 147 J. Immunol. 2964 (1991) (Exhibit B), the authors described the requirement for a D-X sequence, along with particular flanking sequences, as a unique substrate for ICE (caspase) and quantified the effects of amino acid substitutions or deletions within the cleavage recognition sequence on cleavage activity.

Consequently, the Applicants contend that they did not randomly select peptides of the prior art and insert them into the instant invention as the Examiner stated. On the contrary, because (1) the specification discloses caspase as a potential target enzyme, (2) the specification discloses cleavage of the blocking moiety by a target protease such as caspase, (3) the prior art precisely describes a range of characteristics that make a peptide a suitable substrate for caspase cleavage, a person of ordinary skill in the art would recognize the characteristics for which the selected peptides were chosen as compatible

with the instant invention. As a result, under *Capon* and *Barr*, the Applicants are not required to list specific sequences in the written description to demonstrate possession of the invention.

Moreover, the Applicants respectfully submit that the Examiner did not meet the requisite burden of providing evidence or reasons why a person skilled in the art would not recognize the claimed invention in the disclosure. M.P.E.P. § 2163.04 states that "[t]he examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." (citing 541 F.2d at 265, 191 USPQ at 98). See also Ex parte Sorenson, 3 USPQ2d 1462, 1463 (Bd. Pat. App. & Inter. 1987).

Specifically, the Examiner stated that "there is no indication in the instant disclosure that [selected peptides] are compatible with the instant invention." The Examiner also stated that "what the reader extracts from the claims/specification is a desire, plan, or first steps for obtaining a desired result." However, in light of the Sleath et al. and Howard et al. references described above, the Examiner's statements do not give a reason why a person of ordinary skill in the art would not recognize the characteristics that make a peptide compatible with the invention.

As a result, the Applicants respectfully request that the Examiner withdraw the instant rejection.

3. The Examiner Mistook the Language of the Disclosure in Asserting That It Is Not Consistent With the Claims.

The Examiner stated that the claims are not consistent with the disclosure because the specification only disclosed caspases 3, 5, and 8; yet, the claims claimed caspase 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10. However, the Applicants respectfully point out that the disclosure at page 22, lines 19-31 in fact reads: "caspases, such as caspase-3, -5, -8, and other caspases of the apoptotic pathway, and interleukin-converting enzyme (ICE)." Therefore, the claims are consistent with the disclosure because the disclosure references all caspases and merely specifies caspase -3, -5, and -8 as examples.

Claim Rejection Under 35 U.S.C. § 112 Second Paragraph

The Examiner rejected claim 30 based on indefiniteness. The Applicants have amended the claim to indicate that it refers to "a method for acquiring an image." Because the amendment enhances the technical clarity of the claim, the Applicants submit that the basis for rejection has been removed.

Claim Rejection Under 35 U.S.C. § 103

1. The Prior Art Does Not Possess the Characteristics of the Claimed Product.

The Examiner states that claim 22 is directed to a product which is comprised of components that are disclosed in Gries et al. However, the Applicants respectfully submit that the components in the prior art invention do not possess the same characteristics as the claimed product; hence, the instant claims are patentable.

MPEP § 2112.01 states that:

> Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). ... [However], the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433. See also Titanium Metals Corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985).

The Examiner stated that "claim 22 is directed to a product comprising a chelator, gadolinium metal, linker, and peptide." The Examiner based the rejection on the contention that the Gries et al. reference discloses the same composition as the claimed invention. However the Applicants submit that the characteristic which is essential to patentability in the instant case, a peptide which is cleavable by caspase and thereby able to regulate the changing of T1 of the MRI agent, is not a characteristic possessed by the Gries et al. product.

In fact, as previously explained in the May 18, 2006 response, Gries et al. teaches away from the instant invention. M.P.E.P. § 1504.03(III) states that:

> A prima facie case of obviousness can be rebutted if the applicant...can show that the art in any material respect 'taught away' from the claimed invention...A reference may be said to teach away when a person of ordinary skill, upon reading the reference...would be led in a direction divergent from the path that was taken by the applicant. (citing In re Haruna, 249 F.3d 1327, 58USPQ2d 1517 (Fed. Cir. 2001)).

Gries et al. teaches away from peptides that may be cleaved by the target enzyme, as such cleavage would render the Gries et al. invention unsuitable for its intended targeting function. In contrast, the key characteristic of the claimed invention is that it **is** cleaved by the target enzyme (caspase). Therefore, the prior product cannot possess the characteristics of the claimed product. Moreover, a person of ordinary skill, upon reading the Gries et al. reference, would be led to use a peptide that **is not** cleaved by the target enzyme, which is a direction divergent from the use of a peptide that **is** cleaved by the

target enzyme as claimed by the Applicants. As such, the Applicants have presented the requisite evidence to rebut the presumption of anticipation and obviousness under M.P.E.P. § 2112.01.

2. Functional Language May Constitute the Point of Novelty Between the Applicant's Claim and the Prior Art.

The Examiner states that a product is not separable from its properties, and therefore where the prior art discloses the components of Applicant's product, it does not have to specifically state how and why T1 changed to anticipate the instant claim. However, the Applicants respectfully submit that the components of the claimed invention possess a unique functional characteristic that is not present in the prior art, i.e., a blocking peptide that is cleavable by the target enzyme to produce a change in T1. Therefore, the claimed invention's unique function constitutes a point of novelty over the prior art.

In *In Re Swinehart*, the court held that a composition of matter claim with a functional limitation was proper where it constituted the point of novelty between the applicants' claim and the prior art. The claim at issue in *Swinehart* read "[a] new composition of matter, transparent to infra-red rays and resistant to thermal shock, the same being a solidified melt of two components..." *Id.* at 227. In particular, the novel limitation, "transparent to infra-red rays," was rejected by the Examiner and the Board as improper functional language. *Id.* at 227-28. The C.C.P.A. disagreed, explaining that:

> Our study of these cases ... satisfies us that any concern over the use of functional language at the so-called 'point of novelty' stems largely from the fear that an applicant will attempt to distinguish over a reference disclosure by emphasizing a property or function which may not be mentioned by the reference and thereby assert that this claimed subject matter is novel. Such a concern is not only irrelevant, it is misplaced .... [W]here the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on. *Id* at 228-29.

In the instant case, the Applicants have claimed a composition of matter using the functional limitation "such that the T1 of said MRI agent is changed" as a point of novelty distinguishing the claims from the prior art. There is no indication that the prior art reference cited by the Examiner, Gries et al., possesses this characteristic.

Gries et al. discloses complex salts for use in NMR, X-ray, and/or ultrasonic diagnosis. Gries et al also discloses that the complexing acids can be coupled as conjugates with biomolecules, including peptides, that are known to concentrate in the organ or part of the organ to be examined. However, Gries does not teach that the peptide is cleaved; rather, Gries teaches away from cleaving the peptide by stating that the peptide must remain coupled to the agent for its intended targeting function. In the

instant application, the novelty of the claimed invention stems from the fact that cleavage of the peptide is required to cause the T1 of the MRI agent to change.

Therefore, the functional point of novelty is not inherent in the prior art referenced in Gries. Consequently, under *Swinehart* the Applicants' use of functional language is perfectly acceptable because it is necessary to distinguish the claims from the prior art. *See Swinehart* at 228-29.

CONCLUSION

In view of the foregoing, it is believed that all claims now pending in this application are in condition for allowance. Should the Examiner not agree, the Applicants respectfully ask the Examiner to contact the undersigned at 415-442-1379 (direct line) to discuss any remaining issues and accelerate the examination and allowance of this application. Authorization is granted to charge any outstanding fees due at this time for the continued prosecution of this matter to Morgan, Lewis & Bockius LLP deposit account No. 50-0310 (Client Matter No. _____ [Former docket No. A-58634-6; 468081-16]).

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Victoria Poulsen

Respectfully submitted,

Dated: 2/6/07
Customer No.: 67374

By: /Robin M. Silva/
Robin M. Silva, Reg. No. 38,304
Filed under 37 C.F.R. §1.34

MORGAN, LEWIS & BOCKIUS LLP
One Market, Spear Street Tower
San Francisco, California 94105
Tele: 415-442-1000
Fax: 415-442-1001
Email: rsilva@morganlewis.com